Remarks

Claims 1-11 and 13-41 are pending in the present application. Claims 24-41 were previously withdrawn following a restriction requirement. Upon entry of the present amendments, claims 7-9 and 13 are hereby canceled. Claims 1-3, 6, and 14 are amended in this paper. Accordingly, claims 1-6, 10, 11, 14-23 are presented for reconsideration.

Interview Summary

On September 20, 2007, Applicant's attorneys Leeck and Rabe conducted a telephonic interview with Examiners Foster and Le. Drs. Heisler and Sutton, representatives of the assignee, also took part in the conference call. The various rejections were discussed including the Office's rejections related to obviousness. Although no agreement was reached in the interview, the present amendments and arguments are based on that discussion and the Examiners' helpful comments.

Claim Objections

In the paper mailed April 10, 2007, the Office objected to various informalities in claims 3, 6-9, 13-14, 18 and 21. Those informalities have been addressed by Applicant as follows.

The Office objected to the phrase "a nucleic acid analogs" in claim 3. In response, Applicant has amended claim 3 to correct the apparent syntax issue.

Claims 6-9 were objected to because they apparently did not make clear that the "peptide moiety" or "antibody" is the "receptor" referred to in claim 1. Claims 7-9 are presently canceled and claim 6 has been amended to clearly recite that the "antibody" is indeed the "receptor" referred to in claim 1.

Claim 8 was objected to as failing to further limit the subject matter of a previous claim. Applicant has canceled claim 8; the subject matter of claim 8 has been incorporated into amended claim 6, described above.

Claim 13 was objected to for grammatical reasons. Applicant has presently canceled claim 13 in view of amended claim 1.

Claim 14 was objected to because of the phrase "the receptors in the affinity substrate." Claim 14 has been amended herein to parallel claim 1 in the recitation of "receptors comprised by the affinity substrate."

The Office objected to claims 18 and 21 due to a line spacing issue. Applicant has corrected this clerical issue in the present claim listing.

Claim Rejections under sec. 112, first paragraph - Written Description

The Office rejected claims 1-11 and 13-23 as failing to comply with the written description requirement. In particular, the Office took issue with Applicant's prior amendment which introduced the term "detection substrate" into the claimed subject matter. The Examiner expressed some confusion as to whether the "detection surface", present in the as-filed claims, should be interpreted as a distinct component or part relative to the "detection substrate."

In response, Applicant has amended claim 1 to remove the "detection substrate" phrase. Specifically, step (b) of claim 1, as amended, calls for "a detection surface, wherein the ligand which is bound to the receptor is transferred to the detection surface." The "detection substrate" phrase has been removed and the relationship between affinity substrate, detection surface and ligand more clearly set forth. Support for this amendment is found throughout the as-filed specification, e.g., see the description under the section heading "Detection Surface", particularly paragraph [0090] detailing the use and advantages associated with various detection surfaces.

As Applicant's amendment removes the offending terminology, and the present amendment is fully supported by the specification, the Office's rejection relating to new matter should be reconsidered and withdrawn.

The Office has further rejected claim 1 based on Applicant's recitation of a method of detecting "at least one ligand" using an affinity substrate that comprise an array of receptors, wherein each receptor is capable of specifically binding to "a ligand." Applicant has presently deleted language related to "an array of receptors" in amended claim 1 and has replaced the preamble language "at least one ligand" with " a ligand." Specifically, step (a) of claim 1, as amended, now calls for a step of "contacting a sample having a ligand with an affinity substrate, wherein the affinity substrate comprises a receptor capable of specifically binding said ligand, the receptor binding the ligand upon contact with the sample." Such amendments appear to

remedy the alleged written description issue raised by the Office and, furthermore, the present amendments are supported by the originally-filed specification, see, e.g., original claim 1 and paragraphs [0015] and [0016] which teach a method including the step of contacting a sample having or suspected of having a ligand with an affinity substrate, wherein the affinity substrate comprises a receptor capable of specifically binding to the ligand.

Accordingly, the Office's rejection to claim 1 as representing a broadening amendment not supported by the original disclosure and claims should be reconsidered and withdrawn.

The Office further alleges that previously-amended claims 1-11, 13, and 15-23 incorporate new matter because of the recitation of receptors capable of binding to "a ligand" would encompass scenarios in which multiple, different receptors all having specificity for the same ligand are used, which the Office believes represents a departure from the originally filed specification and claims.

Applicant believes that the present amendments to claim 1, as described above, alleviate this rejection because reference to "an array of receptors capable of specifically binding to a ligand" has been removed and replaced with clarifying language fully supported by the originally filed specification and claims. Again, amended claim 1 now recites a step of "contacting a sample having a ligand with an affinity substrate, wherein the affinity substrate comprises a receptor capable of specifically binding said ligand, the receptor binding the ligand upon contact with the sample", which is supported by at least original claim 1 and paragraphs [0015] and [0016] of the specification.

Remaining claims 2, 4-6, 10, 11, and 18-23, which depend from claim 1, are believed to recite subject matter further defining the claimed invention over the art. Therefore, the Office's rejection related to alleged new matter, as set forth at paragraph 20 of the paper mailed April 10, 2007, should be reconsidered and withdrawn.

Claim Rejections under sec. 112, second paragraph - Indefiniteness

Claims 1-11 and 13-23 stand rejected by the Office under sec. 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim Applicant's invention. In particular, the Office has taken issue with the phrase "the ligand" in claim 1 and concluded there is insufficient antecedent basis for this limitation. In response, Applicant has amended claim 1 to

better clarify that the ligand present in the sample is indeed the ligand that is specifically bound by the receptor present on the affinity substrate. The "at least one" ligand language has also been removed to further clarify the relationship between the ligand present in the sample and the ligand specifically bound by the receptors present on the affinity substrate; i.e., the recited "ligand" is, in fact, the one and the same throughout presently amended claim 1. The similar rejection to claim 9 has been rendered moot by the cancellation of claim 9.

Similarly, the Office alleges that the term "the receptor" in claim 1 lacks antecedent basis because the claims refer to an "array of receptors" and not to a receptor per se. In view of Applicant's amendment of claim 1, particularly the deletion of the "array" language, this rejection is overcome and should be withdrawn.

Referring to paragraph 26 of the paper mailed April 10, 2007, the term "peptide moiety" in claims 6-8 also raised a clarity issue with the Office because the Office believed "peptide moiety" did not properly encompass "antibody." Applicant has cancelled claims 7 and 8 and amended claim 6 to recite that "the PDMS of the affinity substrate is further terminated by an antibody which acts as the receptor capable of specifically binding said ligand, the antibody binding the ligand upon contact with the sample." The offending term "peptide moiety" has therefore been removed and, in addition, the relationship between the antibody, PDMS, and affinity stamp has been explicitly set forth.

Finally, the Office's rejection to claim 13 as it relates to the phrase "the receptor-bound ligand", set forth at paragraph 27 of the paper mailed April 10, 2007, has been rendered moot as claim 13 and its subject matter has been canceled by Applicant.

In view of the above described amendments and remarks, the Office's rejections under sec. 112, second paragraph, have been overcome and reconsideration is respectfully requested.

Claim Rejections under sec. 103 - Obviousness

The Office has rejected claims 1-6, 8-11, 13, 15-20 and 22-23 as obvious over Bernard et al. or, alternatively, Renault et al. in view of Abbott et al. (U.S. Patent 6,284,197).

In making a rejection under sec. 103, the Office must articulate a reason or rationale to support that obviousness rejection. That reason or rationale should be based on the state of the art and not on impermissible hindsight using the Applicant's disclosure. In making an

obviousness rejection, the Office may base its rationale on whether: (a) there is some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to the artisan to modify the references; (b) the artisan would have a reasonable expectation of success; and (c) the prior art references teach or suggest all of the claim limitations.

An obviousness rejection may further find proper rationale if all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time to the invention. In certain cases, an obviousness conclusion may be reached where a simple substitution of one known element for another was carried out to arrive at the claimed subject matter and the substitution yielded only a predictable result. As well, an obviousness rejection' rationale is proper where the claimed subject matter was arrived at by Applicant's choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. However, the Office's rationale for making its obvious rejections in the present case is unfounded in view of the lack of teachings/guidance provided in the cited references or any general knowledge available to the artisan at the time of the invention and, as well, the lack of any expectation of success and predictability by the artisan upon combining prior known elements.

In the paper mailed April 10, 2007, the Office relies upon Bernard et al. to teach a method of detecting a ligand comprising the step of (a) contacting a sample having a ligand (e.g., ^{125}I-IgG) with an affinity substrate (PDMS stamp) wherein the affinity substrate comprises an array of receptors that are capable of specifically binding the ligand. The Office further alleges that Bernard et al. teach a step (b) of contacting the affinity substrate with a detection surface (glass or polystyrene) wherein a portion of the ligand that is bound by the receptor is transferred to the detection surface. Bernard et al. apparently fail to teach detection of the ligand on the detection surface by liquid crystal but, instead, utilize radioactive or fluorescent labels attached to the target ligands. No further teaching as to selection of suitable detection surfaces is provided, and certainly no expectation of success for combining affinity microcontact printing with liquid crystal detection is indicated.

In similar fashion, Renault et al. is relied upon by the Office to teach a method of detecting a ligand (e.g., an antibody) by contacting a ligand-containing sample with an affinity substrate (PDMS stamp), followed by transfer of the ligand to a detection surface where detection of the ligand is accomplished by fluorescent or gold-labeled antibodies via fluorescence microscopy or atomic force microscopy. Renault et al. fail to teach detection of the ligand via liquid crystal techniques. Like Bernard et al., Renault et al. includes no further teaching or indicator of success for combining affinity microcontact printing and liquid crystal detection.

The Office relies on Abbott et al. to teach a device having a detection surface to which a ligand may be transferred and its presence subsequently detected by using a liquid crystal. The Office states one of skill would have been motivated to combine the teachings of Bernard et al. and Abbott et al. or, alternatively, Renault et al. and Abbott et al., because Abbott et al. teach that liquid crystal detection surfaces do not require prelabeling of the ligand and, as such, one would be motivated to stamp the affinity-captured ligand onto the device of Abbott et al. in order to avoid the need for fluorescent or labels of the ligands. The Office further states that "one would have a reasonable expectation of success in affinity stamping the surface of Abbott et al. according to the methods of Bernard et al. or Renault et al. because the surface of Abbott et al. is compatible with microcontact printing. The Office refers Applicant to the reference by Abbott et al. at column 17, lines 5-22 to support this conclusion.

As presently amended, claim 1 recites a method for detecting a ligand in a sample comprising: (a) contacting a sample having a ligand with an affinity substrate, wherein the affinity substrate comprises a receptor capable of specifically binding said ligand, the receptor binding the ligand upon contact with the sample; (b) contacting the affinity substrate with a detection surface, wherein the ligand which is bound to the receptor is transferred to the detection surface; and (c) detecting the presence of the ligand on the detection surface by contacting the detection surface with a liquid crystal, wherein the presence of the ligand on the detection surface is detected by a change in the orientation of the liquid crystal contacted with the detection surface. The subject matter of amended claim 1 is fully supported in the as filed specification, e.g., reference may be made to paragraph [0090] of the originally filed

specification where Applicant describes, among other things, detection surfaces for use in the transfer of protein from affinity substrate to detection surface.

Keeping Applicant's claimed subject matter in mind, it is apparent that Bernard et al. do not teach nor do they suggest the use of a detection surface upon which a ligand may be stamped and liquid crystal detection subsequently carried out. Bernard et al. are limited in their teaching to the use of a polystyrene substrate for affinity stamping. As well, Renault et al. fail to teach or suggest the presently claimed elements and only teach glass as a stamping substrate. Combining affinity microcontact printing with liquid crystal detection is simply not contemplated by these two cited references; no teaching is provided by Bernard et al. and Renault et al. to guide an artisan in the context of liquid crystal detection. The successful detection of affinity stamped ligand on a detection surface by liquid crystal, as opposed to ligand detection by fluorescent or radioactive labeling, is far from a mere substitution of one known element for another to obtain predictable results.

While the cited reference to Abbott et al. describes a wide variety of surfaces suitable for liquid crystal detection, including a general mention of self assembled monolayers, the method of detecting affinity microcontact printed ligands via detection surfaces compatible with liquid crystals is not disclosed or suggested by Abbott et al. At most, Abbott et al. recognizes various materials that may be used in the practice of liquid crystal detection and does not show or suggest that detection surfaces may also act to receive a ligand to be detected from an affinity substrate.

In arriving at its conclusion that the detection surface of Abbott et al. is compatible with affinity microcontact printing, the Office cites to column 17, lines 5-22 of the reference to Abbott et al. where mention to microcontact printing is made in the context of patterning a detection surface (termed a "detection substrate"). It should be noted that "affinity" microcontact printing is not mentioned in the Abbott et al. reference. In fact, the transfer of a ligand to be detected by any microcontact printing technique is not described by Abbott et al. Instead, Abbott et al. discuss microcontact printing in the context of forming patterns ("as small as 200 nm") such as, "wells, enclosures, partitions, recesses, inlets, outlets, channels, troughs, diffraction gratings and the like." The discussion of microcontact printing by Abbott et al. is, in fact, in an unrelated context to the transfer of ligand by "affinity" microcontact printing taught by Bernard

et al. and Renault et al. Therefore, the Office's contention that the detection surfaces taught by Abbott et al. are generally compatible with affinity microcontact printing in that the artisan would expect success in ligand detection via liquid crystal methodology is unfounded.

In order to aid the Office in its appreciation of this central issue, Inventor Abbot has submitted a statement in a Declaration under Rule 1.132 accompanying this paper. The Examiner is referred to paragraphs 5 and 6 of the accompanying declaration where Dr. Abbott addresses the discussion of microcontact printing in U.S. Patent 6,284,197, in which he was a co-inventor. Dr. Abbott clearly indicates that the previous teaching regarding microcontact printing was in the context of fabricating detection surfaces, a pre-detection activity. In contrast, the presently claimed invention is directed to using a specific type of microcontact printing, namely affinity microcontact printing to carry out delivery of a ligand to be analyzed by a detection surface. The substitution of the detection methods described in his previous patent (i.e., the Abbott et al. reference) for fluorescent or radioactive labeling described by Renault et al. and Bernard et al. would not have been prompted by design incentives as the artisan, after considering the cited references and general knowledge, would not have predicted a successful result due to the lack of available guidance in the art for combining affinity microcontact printing with liquid crystal detection. Applicant respectfully maintains that the Office's rationale is based on impermissible hindsight analysis using the Applicant's disclosure.

In summary, there is simply no teaching, suggestion, or motivation in the cited references or in the knowledge generally available to the artisan that would have led the artisan to combine the prior art teachings to arrive at the claimed invention. Dr. Abbott's statements regarding the various surfaces described in the cited references further support Applicant's position that there would have been no reasonable expectation of success upon combining the prior teachings. Based upon the present amendments, inventor's declaration, and the above argument, the Office's obviousness rejection should be reconsidered and withdrawn. Claims 2-6, 8-11, 13, 15-20 and 22-23 depend from amended claim 1 and are therefore believed to recite additional elements which define the claimed invention over the prior art.

The Office has further held claims 7 and 14 as obvious over Bernard et al. or Renault et al. in view of Abbott et al, and further in view of Tang et al. (U.S. Patent 5,886,195).

Tang et al. is relied upon by the Office to allegedly teach anti-phosphotyrosine antibodies, which may be used to measure autophosphorylation of EGFR and thereby an increase in EGF activity. The Office believes it would have been obvious to the artisan to employ the anti-phosphotyrosine antibodies taught by Tang et al. as the receptor molecules on the affinity substrate in a method for detecting a ligand based on Bernard et al. and Abbott et al. or, alternatively, Renault et al. and Abbott et al. However, the Tang et al. reference fails to cure the deficiencies in Bernard et al., Renault et al., and Abbott et al., as discussed above. Tang et al. and the additional references simply do not teach nor do they contemplate a ligand detection method having an affinity microcontact stamping step combined with a ligand detection step of contacting liquid crystal with a detection surface. In view of Applicant's arguments and amendment of claim 1, from which claim 14 depends, and the cancellation of claim 7, this rejection should be reconsidered and withdrawn.

Finally, the Office found claim 21 obvious over Bernard et al. or Renault et al. in view of Abbott et al, and further in view of Choi et al. (U.S. Patent 6,292,296).

Choi et al. is relied upon by the Office for the apparent disclosure of photo-alignment in liquid crystal devices. However, the Choi et al. reference fails to cure the previously discussed deficiencies in Bernard et al., Renault et al., and Abbott et al. Choi et al. and the additional references simply do not teach nor do they suggest a ligand detection method having an affinity microcontact stamping step combined with a ligand detection step of contacting liquid crystal with a detection surface. In view of Applicant's arguments and amendment of claim 1, from which claim 21 depends, this rejection should be reconsidered and withdrawn.

Nonstatutory Obviousness-type double patenting - Provisional rejections

The Office has provisionally rejected claims 1-11 and 13-23 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application 11/542,432 in view of Renault et al. Applicant wishes to point out that the cited co-pending application is not commonly-owned with the present application.

In addition, the Office has provisionally rejected claims 1-11 and 13-23 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of copending Application 11/418,755 in view of Renault et al.

As both double patenting rejections are provisional in nature and no conflicting claims have yet been patented, Applicant acknowledges these issues but does not respond further at this time.

Conclusions

In view of the present amendments and remarks presented herein, Applicant respectfully submits that claims 1-6, 10, 11, 14-23 are in condition for allowance and notice to that effect is earnestly solicited. The Examiner is urged to telephone the undersigned in the event a telephone discussion would be helpful in advancing the prosecution of this case. The Office is authorized to charge the extension fee, or any other surcharges or underpayment associated with this filing, as deemed necessary and appropriate, to Deposit Account 17-0055.

Respectfully submitted,

WISCONSIN ALUMNI RESEARCH FOUNDATION

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